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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,871	02/20/2004	Bonnie Hepburn	29635-714.201	7593

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EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/783,871	HEPBURN ET AL.	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,19 and 60-70* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicants' response, filed 4/20/2009, to the Office Action mailed 10/20/2008 is acknowledged. Applicants canceled Claims 1-17 and 20-33 and 52-59, amended Claims 60-69, added Claim 70, and presented arguments in response to the Office Action.

2. Claims 18, 19, and 60-70 are pending.

3. Claim 60-70 are presently under consideration.

4. Applicants' arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 60-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (U.S. Patent No. 6,489,346 B1), in view of Hatlebakk et al. (Alimentary Pharmacology and Therapeutics, 2000, Vol. 14, pages 1267-1272).

Phillips teaches a pharmaceutical composition comprising a non-enteric coated proton pump inhibitor, in an amount of approximately 5 mg to approximately 300 mg, and a least one buffering agent, in an amount of approximately 0.1 mEq to approximately 2.5 mEq per mg of proton pump inhibitor. See Abstract. Phillips teaches the composition can be formulated as a powder, tablet, suspension tablet, chewable tablet, capsule, effervescent powder, effervescent tablet, pellets and graduals and liquids. The buffering agent is utilized to protect the proton pump inhibitor against gastric acid degradation. See column 11 lines 13-32. Phillips teaches omeprazole/sodium bicarbonate formulations wherein omeprazole is present in the formulation in the amount of 5 mg, 10 mg, 20 mg, 40 mg, 60 mg, 80 mg and 100 mg. See column 39, claim 1 and column 41, claims 36-41. The reference further teaches the formulation buffering agent (i.e., sodium bicarbonate) is present in the amount of 400 mg to 4000 mg. See column 42, claim 59. The proton pump inhibitor can be an

enantiomer, isomer, derivative, free base or salt of the parent compound. See column 42, claim 57. Phillips teaches the proton pump inhibitor can be micronized. See column 41, claim 49. The composition taught further comprises excipients, including flavoring agents, diluents, disintegrants, lubricants, preservatives and lubricants. See column 44, claim 116. Furthermore, Phillips teaches methods of treating gastrointestinal conditions, including GERD, by administration of the proton pump inhibitor/buffer formulations described above (including omeprazole/sodium bicarbonate). See column 12, lines 39-49.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). Phillips teaches proton pump inhibitor/buffering agent compositions that are identical to those recited by the instant invention (*supra*). Therefore, the pharmacokinetic and pharmacodynamic characteristics of the compositions taught by Phillips would be the same as those recited by the instant claims. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d

1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Phillips does not disclose *per se* the administration of the proton pump inhibitor compositions within about 60 minutes prior to a meal, as required by the instant claims.

Hatlebakk et al. teach the administration of the proton pump inhibitors, omeprazole and lansoprazole, 15 minutes prior to a meal, to provide better acid suppression. See page 1267, "SUMMARY".

One skilled in the art of pharmaceutical formulation is provided with guidelines from Phillips, sufficient to prepare formulations comprising a proton pump inhibitor, such as omeprazole, in combination with a buffer, such as sodium bicarbonate, to treat patients suffering from GERD. The reference teaches or suggests each limitation of the present claims. It is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See In re Aller, 220 F.2d 454, 456, 105 USPQ233,235 (CCPA 1955) and MPEP 2144.05(11). The determination of the optimum dosages, particle sizes, gastric fluid pH ranges, serum concentrations over time and drug release rates to employ or to seek with the presently claimed agents, would have been a matter well within the purview of one of ordinary skill in the art. Such determination would have been made in accordance with a variety of factors. These would have included such factors as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration,

pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, in the absence of evidence to the contrary, the currently claimed specific dosage amounts, particle sizes, serum concentrations over time and drug release rates are not seen to be inconsistent with those that would have been determined by the skilled artisan.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Phillips with those of Hatlebakk et al. The teaching of Hatlebakk et al. that administration of proton pump inhibitors 15 minutes prior to a meal improves acid suppression would have motivated one to do so; to provide an improved treatment of GERD symptoms.

8. Claims 60-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (U.S. Patent Application Pub. No. 2003/0191159 A1), in view of Hatlebakk et al. (*Id.*).

Phillips teaches methods and compositions for treating gastric acid disorders, including *inter alia* GERD and heartburn, employing pharmaceutical compositions comprising an acid labile proton pump inhibitor and a buffering agent. See Abstract, and page 11, paragraph 100, and page 54, claim 122. Phillips teaches the composition can be formulated as a powder, tablet, suspension tablet, chewable tablet, capsule, effervescent powder, effervescent tablet, pellets and graduals and liquids. The buffering agent is utilized to protect the proton pump inhibitor against gastric acid

degradation. See page 5, paragraph 37 and page 52, claim 37. Phillips teaches the proton pump inhibitors are present in the composition in amounts from 5 mg to 1000 mg and unit doses of 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 40 mg, 50 mg, 60 mg, 75 mg, 80 mg, or 100 mg. See page 10, paragraphs 84 and 85. The reference teaches the buffering agent present in the composition in an amount of 0.1 mEq to 2.5 mEq per mg of proton pump inhibiting agent. The reference further teaches the formulation buffering agent (i.e., sodium bicarbonate) is present in the amount of 250 mg to 4000 mg. See page 52, claim 26. The proton pump inhibitor can be in the form of a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, and derivative. See page 7, paragraph 65. Phillips teaches the proton pump inhibitor can be micronized. See page 13, paragraph 131. The composition further comprises excipients, including flavoring agents, diluents, disintegrants, lubricants, preservatives and lubricants. See page 53, claim 70. The reference teaches the proton pump inhibitor can be enteric coated or uncoated. See page 5, paragraphs 37 and 38, and page 52, claim 45. The Phillips reference teaches that the composition buffering agent is present in an amount sufficient to increase gastric fluid pH of the stomach to a pH that inhibits acid degradation of the proton pump inhibitor agent in the gastric fluid, so as to allow absorption of the proton pump inhibiting agent and to provide a therapeutically effective serum concentration of the proton pump inhibitor of at least 150 ng/ml within 15 minutes after ingestion of the composition. See page 52, claim 37. Phillips teaches an omeprazole T_{max} of less than 1.5 hours with a C_{max} ranging from 763 ng/ml to 1460 ng/ml for an omeprazole/sodium bicarbonate composition. See page 30, paragraph 325

and Table 9. Phillips further teaches a plethora of additional pharmacokinetic and pharmacodynamic information on proton pump inhibitor/buffering agent compositions. One of skill in the art would recognize that the pharmacokinetic and pharmacodynamic characteristics of a composition are complex and depend upon *inter alia* the age, body weight, general health, and sex of the patient, the rate of excretion, the drug combination and formulation, and the route of administration.

As discussed *supra*, *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). Phillips teaches proton pump inhibitor/buffering agent compositions and methods that are identical to those recited by the instant invention. Therefore, the pharmacokinetic and pharmacodynamic characteristics of the compositions taught by Phillips would be the same as those recited by the instant claims.

Phillips does not disclose *per se* the administration of the proton pump inhibitor compositions within about 60 minutes prior to a meal, as required by the instant claims.

Hatlebakk et al. teach the administration of the proton pump inhibitors, omeprazole and lansoprazole, 15 minutes prior to a meal, to provide better acid suppression (*supra*).

One skilled in the art of pharmaceutical formulation is provided with guidelines from Phillips, sufficient to prepare formulations comprising a proton pump inhibitor, such as omeprazole, in combination with a buffer, such as sodium bicarbonate, to treat patients suffering from GERD. The reference teaches or suggests each limitation of the present claims. It is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See In re Aller, 220 F.2d 454, 456, 105 USPQ233,235 (CCPA 1955) and MPEP 2144.05(11). The determination of the optimum dosages, particle sizes, gastric fluid pH ranges, serum concentrations over time and drug release rates to employ or to seek with the presently claimed agents, would have been a matter well within the purview of one of ordinary skill in the art. Such determination would have been made in accordance with a variety of factors. These would have included such factors as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, in the absence of evidence to the contrary, the currently claimed specific dosage amounts, particle sizes, serum concentrations over time and drug release rates are not seen to be inconsistent with those that would have been determined by the skilled artisan.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Phillips with those of Hatlebakk et al. The

teaching of Hatlebakk et al. that administration of proton pump inhibitors 15 minutes prior to a meal improves acid suppression would have motivated one to do so; to provide an improved treatment of GERD symptoms.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Applicants argue the omeprazole and lansoprazole taught by Hatlebakk et al. are enteric coated, and thus, "significantly different" than the "non-enteric coated" proton pump inhibitor compositions taught by Phillips and instantly claimed. Applicants urge "[t]he Examiner has provided no evidence that one of skill in the art would have been motivated to combine references describing these significantly different compositions together. Nor has the Examiner shown that one of skill in the art would have expected the very different compositions described in the two references cited to have the same benefit if dosed before a meal." Further, Applicants argue it would not have been expected for the compositions taught by Phillips and Hatlebakk et al. to behave similarly

because "the absorption of an enteric coated proton pump inhibitor occurs substantially later than a non-enteric coated proton pump inhibitor."

Applicants' arguments have been fully considered but have not been found persuasive. Hatlebakk et al. teach administration of omeprazole or lansoprazole 15 minutes prior to a meal to provide better acid suppression (supra). Although the dosage forms of omeprazole and lansoprazole used in the administration protocol of Hatlebakk et al. are enteric coated, there is nothing in the disclosure of Hatlebakk et al., or in the arguments presented by Applicants, to suggest the improved acid suppression demonstrated by administration of an enteric coated proton pump inhibitor prior to a meal would not have also occurred using a non-enteric coated proton pump inhibitor. Hatlebakk et al. suggest "omeprazole and lansoprazole inhibit gastric acid secretion by selectively and non-competitively inactivating the H^+, K^+ ATPase molecules of the parietal cell, but possible only those that are actively secreting acid. This might imply that stimulation of acid secretion by a meal is necessary for optimal inhibition of gastric secretion." See page 1267, "Summary: Background" first two sentences. The enteric coating of the formulations used by Hatlebakk et al. would not be expected to influence the beneficial effect of administration prior to a meal demonstrated by Hatlebakk et al.

Conclusion

10. Claims 60-70 are rejected.

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614